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ORIGINAL ARTICLE

Stress and use of over-the-counter analgesics: prevalence and association among Danish 25 to 44-year-olds from 1994 to 2005

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Abstract
Objectives To examine the prevalence of over-the-counter analgesic (OTCA) use and perceived stress among 25 to 44-year-old men and women from 1994 to 2005; to examine the association between stress and OTCA use over time, and to explore whether the association attenuates when controlled by stress-related symptoms.
Methods Cross-sectional studies were carried out in 1994, 2000 and 2005. The study population included men and women from ages 25 to 44 years ($n_{1994} = 1{,}781$, $n_{2000} = 5{,}819$, $n_{2005} = 4{,}831$). The surveys were conducted by face-to-face interviews and the outcome measure was OTCA use. The independent variable was perceived stress and pain/discomfort symptoms were included as covariates.
Results There was a significant increase in OTCA use and often feeling stressed from 1994 to 2005. Although there was a significant association between stress and OTCA use for men in all three surveys, there was no association in 2000 when adjusted for symptoms. For women stress and OTCA use were not associated in 1994, while in 2000 and 2005 the association was significant, also after adjusting for symptoms.
Conclusion The findings indicate that there may be an increasing overuse of OTCA in treating stress among 25 to 44-year-old men and women.

Keywords Medicine use · Over-the-counter analgesics · Pharmacoepidemiology · Stress · Young adults

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Introduction

Although the primary reason for using analgesics is headache symptoms (Abbott and Fraser 1998; Antonov and Isacson 1998), not all analgesic use can be explained by the prevalence of symptoms (Abbott and Fraser 1998; Andersen et al. 2009; Hansen et al. 2008; Holstein et al. 2009). Researchers have suggested that some medicine use may be behavior reflecting a general coping strategy to overcome daily stressors over and above therapeutic indications (Due et al. 2007; Hansen et al. 2008; Stasio et al. 2008).

Various types of health and illness behavior, e.g., smoking, drinking and a low level of exercise, are related to stress (Cohen et al. 1991; Nielsen et al. 2008a; Siegrist and Rodel 2006) and findings support the notion of a 'health behavior' model of stress in which populations under stress engage in behavior that is harmful to health (Colby et al. 1994). There is already some evidence that life stress, and psychological distress may be related to the use of non-prescription medications in selected populations (Abbott and Fraser 1998; Stasio et al. 2008 e.g., among Danish slaughterhouse workers (Kristensen 1991), young women (Hansen et al. 2008) or female Finnish conscripts

(Linden et al. 2006). However, our knowledge about psychosocial factors that may affect the use of OTCA in the general population is limited. We recently conducted a national study among Danish 25 to 44-year-olds (Koushede et al. 2010) and found a significant and graded association between stress and OTC analgesic (OTCA) use, i.e., the odds for OTCA use mounted with increasing levels of stress. In this study, the association was not explained exclusively by potential stress-related aches and pains.

Use of this type of medicine to cope with stress must be considered inappropriate, as it is not indicated for this purpose. Overuse of OTCA is a concern because the practice is widespread and may have adverse health effects, e.g., medicine-induced headache (Dyb et al. 2006), gastrointestinal bleeding, liver and kidney failure, and myocardial infarction and death (Sweetman 2009).

Since the 1980s, there has been a significant increase in the use of analgesics as well as in the prevalence of people, at the population level, who report often feeling stressed in their daily lives (Ekholm et al. 2006; The Danish Medicines Agency 2009). If both the determinants, i.e., perceived stress, and the effect, in this case OTCA use, increase over time, the association between the two variables may change as well. Therefore, it is important to study whether the association between stress and OTCA is a new phenomenon or whether the association has been robust over time.

This study focuses on 25 to 44-year-olds because this age group has the highest level of perceived stress (Ekholm et al. 2006) and the highest level of OTCA use (Ekholm et al. 2006).

The primary objective of this study was to examine the prevalence of OTCA use and perceived stress among a representative sample of 25 to 44-year-old men and women between 1994 and 2005, as well as to examine the association between perceived stress and OTCA over time.

It is possible that the effect of stress-related symptoms associated with stress and OTCA use may have altered over the years. Our secondary objective was to examine whether an association between perceived stress (hereafter stress) and OTCA use attenuates in analyses when potential stress-related symptoms are included in the statistical model from the different survey years.

Methods

Design and data collection

We analyzed data from three National Health Interview Surveys (NHIS) conducted in Denmark in 1994, 2000 and 2005 (Ekholm et al. 2009). The surveys were based on random samples of adult Danish citizens (16 years or older). The samples were drawn from the Danish Civil Registration System (each Dane has a unique personal registration number). All selected individuals received a letter of introduction that briefly described the purpose and content of the survey. It was emphasized that participation was voluntary. The surveys were carried out by the National Institute of Public Health, University of Southern Denmark. They consist of a range of validated items on health behavior, working conditions and socio-demographic factors. Data were collected via face-to-face interview at the respondent's home. The design of the surveys is described in detail in Ekholm et al. 2009.

Study population

Our study population included the NHIS participants aged 25 to 44 years. The response rate for this age group was 82.0% in 1994 ($n = 1{,}781$), 75.9% in 2000 ($n = 5{,}819$) and 68.0% in 2005 ($n = 4{,}831$).

Measurements

The outcome variable was OTCA use measured by the item: 'within the past 14 days have you taken any of the following medicines?' There were two OTCA measures: (1) OTCA for discomfort and pain in muscles, bones, tendons or joints, and (2) OTCA for other symptoms. Analyses were conducted for the two types separately and combined. The responses were dichotomized for use or no use. The study focuses on the behavioral aspects of OTCA use, and does not include data about the kind of medicine used.

The exposure variable 'stress' was measured by the item: 'do you feel stressed in your daily life?' The responses were: (1) yes, often; (2) yes, sometimes; (3) no/hardly ever. Single-item stress measures have previously shown satisfactory content, criterion and construct validity (Elo et al. 2003; Hosmer and Lemeshow 2000).

The symptom variables were derived from the question: 'within the past 14 days have you been bothered by any of the following kinds of pain or discomfort?': (1) shoulder or neck; (2) back or lower back; (3) arms, hands, legs, knees, hips or joints; (4) headache; (5) stomachache (response key "yes bothered a lot", "yes, bothered somewhat", "no")'. We combined these data into an index for symptoms: 1 = yes to at least one symptom, otherwise 2.

Education was assessed using the International Standard Classification of Education (ISCED), which combines school and vocational education (UNESCO 1997). We re-coded education into two categories to maintain adequate statistical power for this study. (1) Short: less than 13 years or (2) long: 13+ years.

Stress and medicine use are linked to family structure (Cafferata et al. 1983; McDonough et al. 2002; Payne et al. 2004); therefore, the analysis adjusted for cohabiting status

and whether or not the participants had children were conducted. Cohabiting status was coded as (1) yes: respondents who answered yes to being married, cohabiting or in a registered partnership, and (2) no: individuals who did not answer yes to any of the above. Similarly, responses were coded as (1) yes or (2) no to having children.

Women are more prone to stress than men (Ekholm et al. 2006) and have a higher use of analgesics (Andersen et al. 2009; Antonov and Isacson 1998; Eggen 1994), for which reason all analyses were carried out separately for men and women.

Statistical procedures

We used SAS software version 9.1 for all analyses. First, we inspected the distribution of the employed variables. Differences between men and women were analyzed using χ^2 test. We inspected the distribution of the employed variables over time. Trends from 1994 to 2005 were analyzed by means of the Cochran–Armitage trend test. Direct standardization was used to derive age- and education-adjusted percentages of OTCA use and stress. The study population in 2005 was used as the standard population.

Second, we studied associations in all three surveys separately by means of logistic regression analyses. Initially, we estimated the crude association between perceived stress and OTCA use. Analyses were conducted separately for the two OTCA measures to examine whether the association between stress and OTCA use depended on which of the two measures that was used. As this was not the case, the two OTCA measures were combined. We examined the association between stress and all symptoms and then conducted analyses to examine whether the association between stress and OTCA use attenuates when potential stress-related symptoms were included in the statistical model. The association was adjusted for the symptom variables individually as well as for the index for symptoms. Analyses adjusted for index for symptoms, age, education, cohabiting status and children were performed.

Finally, the three surveys were pooled for each sex and an interaction term, stress × year, was included to test whether the association between stress and OTCA use was statistically robust over time. Statistical significance was assessed using both Wald and likelihood ratio statistics. The tests produced very similar results and, hence, only the results from the Wald statistics are presented in this paper. Goodness of fit of the models was assessed by the Hosmer–Lemeshow test (Hosmer and Lemeshow 2000). The test indicated that the models fit the data adequately. Associations were reported as odds ratios (OR) with 95% confidence intervals (CI).

Results

Tables 1 and 2 show the gender-specific distribution of mean age, OTCA use, perceived stress, symptoms, cohabiting status, children and education in 1994, 2000 and 2005. Significantly more women than men reported in all three surveys: stress, OTCA use within the past 14 days, headache, stomachache and shoulder/neck pain ($p < 0.05$). More

Table 1 Descriptive information on the studied variables among men in Denmark in 1994, 2000 and 2005, in %

Men	1994	2000	2005	Trend test p value
Total (n)	881	2,835	2,313	
Mean age (years)	34.5	34.6	35.0	
OTCA use				
Yes	23.6	22.3	25.9	0.0200
Yes[a]	23.9	22.3	25.8	0.0339
Perceived stress				
Sometimes	43.7	45.6	44.3	
Often	8.4	11.0	11.0	0.0327
Often[a]	9.5	11.3	11.0	0.0779
Headache	16.9	16.3	23.0	<0.0001
Stomachache	4.7	3.9	5.1	0.1294
Shoulder/neck pain	22.4	22.2	27.4	<0.0001
Backache	24.7	23.7	25.8	0.1379
Pain in arms, hands, legs, knees hips or joints	16.1	18.2	23.0	<0.0001
Index for symptoms[b]	54.7	53.8	62.8	<0.0001
Education <13 years	42.7	35.8	30.4	<0.0001
Cohabiting	74.0	73.8	75.8	0.0799
Children	55.3	52.6	56.4	0.0958

[a] Age and education standardized percentages

[b] Yes to at least one pain or discomfort in: shoulder or neck; back or lower back; arms, hands, legs, knees, hips or joints; headache; stomachache

Table 2 Descriptive information on the studied variables among women in Denmark in 1994, 2000 and 2005, in %

Women	1994	2000	2005	Trend test p value
Total (n)	900	2,984	2,426	
Mean age (years)	34.5	34.6	35.2	
OTCA use				
Yes	33.6	35.1	37.0	0.0217
Yes[a]	34.5	35.2	37.1	0.0349
Perceived stress				
Sometimes	48.2	49.0	46.8	
Often	10.4	12.3	14.2	0.0010
Often[a]	11.3	12.5	14.2	0.0023
Headache	25.9	30.4	38.1	<0.0001
Stomachache	7.8	7.1	10.4	0.0004
Shoulder/neck pain	35.9	35.4	41.6	<0.0001
Backache	26.1	26.3	32.6	<0.0001
Pain in arms, hands, legs, knees hips or joints	18.3	18.7	27.5	<0.0001
Index for symptoms[b]	66.3	67.7	75.0	<0.0001
Education <13 years	34.3	25.1	18.8	<0.0001
Cohabiting	80.0	79.1	79.4	0.4065
Children	66.0	67.2	69.5	0.0147

[a] Age and education standardized percentages

[b] Yes to at least one pain or discomfort in: shoulder or neck; back or lower back; arms, hands, legs, knees, hips or joints; headache; stomachache

women than men reported backache [significant in 2000 and 2005 ($p < 0.05$)] and pain in arms, hands, legs, knees hips or joints [significant in 2005 ($p < 0.05$)]. There was a significant increase in all symptoms among women between 1994 and 2005. Among men, there was a significant increase in all symptoms apart from stomachache and backache. From 1994 to 2005, there was a significant increase in OTCA use and often feeling stressed among men and women ($P_{\text{OTCAmen}} = 0.0200$, $P_{\text{OTCAwomen}} = 0.0217$, $P_{\text{stressmen}} = 0.0327$, $P_{\text{stresswomen}} = 0.0010$). OTCA use was reported by 23.6% of the men and 33.6% of the women in 1994 and by 25.9% of the men and 37.0% of the women in 2005. In 1994, 8.4% of men and 10.4% of women reported often feeling stressed compared to 11.0% of men and 14.2% of women in 2005. After standardizing for age and combined school and vocational education (ISCED), the increase in OTCA use and in often feeling stressed were fairly unchanged. However, the increase in often feeling stressed among men was no longer significant ($p = 0.0779$).Among participants not reporting any symptoms, approximately 11% of women and 10% of men reported OTCA use. Among participants who reported OTCA use, between 33 and 41% of the women and just fewer than 40% of the men reported often feeling stressed (results not shown).

Stress was significantly associated with the symptoms headache, stomachache, and shoulder or neck pain among both men and women in all three surveys. With the exception of women in 1994, stress was significantly associated with back pain. Among men, there was no association between stress and pain in arms, hands, legs, knees, hips or joints in any of the surveys (results not shown).

As seen in Table 3, there was a significant and graded association between stress and OTCA use among men in all three surveys, i.e., the odds for OTCA use mounted with increasing levels of stress. There was a strong association between stress and OTCA use in 1994 and 2005, which remained after adjusting for the index for symptoms, age and education (Model III). In 2000, the association between stress and OTCA use was weaker, and it vanished when adjusted for symptoms, age and education. Among women there was a strong association between stress and OTCA in the surveys of 2000 and 2005, but no association in the survey of 1994. In analyses adjusted for index for symptoms, age and education, the association between stress and OTCA use in 2000 and 2005 remained significant and graded. Adjustment for cohabiting status and whether the respondents had children barely altered the association between stress and OTCA use for men or women; therefore, these results are not presented.

In analyses individually adjusted for symptoms, headache was the symptom that most notably attenuated the association between stress and OTCA use in all three surveys for both men and women (Table 3 model II).

The interaction between year, stress and gender was statistically non-significant ($p = 0.6404$).

Discussion

From 1994 to 2005, there was a significant increase in OTCA use and in reports of often feeling stressed among men and women (among men the increase in often feeling

Table 3 OR (95% CI) for OTCA use in relation to stress (reference level = never) among men and women in Denmark in 1994, 2000 and 2005

	Men			Women		
	Model I	Model II	Model III	Model I	Model II	Model III
1994 stress						
Sometimes	**1.66** (1.19–2.33)	1.44 (0.98–2.11)	**1.47** (1.03–2.10)	0.99 (0.74–1.32)	0.82 (0.59–1.15)	0.88 (0.64–1.21)
Often	**2.93** (1.73–4.98)	**1.96** (1.04–3.67)	**2.14** (1.20–3.79)	1.02 (0.63–1.64)	0.70 (0.40–1.22)	0.67 (0.40–1.21)
p	<0.0001	0.0518	0.0155	0.9917	0.3399	0.2862
2000 stress						
Sometimes	1.18 (0.98–1.43)	1.08 (0.88–1.33)	1.08 (0.88–1.31)	1.13 (0.96–1.33)	0.97 (0.81–1.17)	1.06 (0.89–1.26)
Often	**1.41** (1.06–1.87)	0.99 (0.71–1.38)	1.14 (0.85–1.53)	**1.85** (1.46–2.35)	**1.47** (1.13–1.92)	**1.51** (1.17–1.95)
p	0.0388	0.7241	0.6276	<0.0001	0.0057	0.0056
2005 stress						
Sometimes	**1.30** (1.07–1.58)	1.21 (0.97–1.51)	1.23 (1.00–1.52)	**1.33** (1.12–1.59)	1.12 (0.92–1.37)	1.14 (0.94–1.38)
Often	**1.96** (1.47–2.62)	**1.48** (1.06–2.07)	**1.65** (1.21–2.23)	**1.77** (1.38–2.26)	**1.43** (1.08–1.90)	**1.40** (1.08–1.82)
p	<0.0001	0.0456	0.0042	<0.0001	0.0450	0.0398
Year × stress interaction	0.1140	0.2317	0.1704	0.0984	0.1324	0.0733

Model I, crude OR; Model II, adjusted for headache; Model III, adjusted for index for symptoms (yes to at least one of the symptoms: pain or discomfort in shoulder or neck; pain in back or lower back; pain in arms, hands, legs, knees, hips or joints; headache; stomachache), age and education

OR values in bold are statistically significant, $p < 0.05$

stressed was no longer significant when standardized for age and education). We found a significant and graded association between stress and OTCA use among men in all three surveys and among women in 2000 and 2005. This pattern remained after adjusting for symptoms, age and education with the exception of men in 2000. There was no statistically significant change in the association between stress and OTCA use over time in spite of the increase in stress and OTCA use. The results indicate that the association between stress and OTCA use is real and not merely explained by stress-related symptoms and that OTCA may be used beyond indication to treat perceived stress.

Abbott and Fraser (1998) found that to a large extent, OTC medicines, primarily analgesics, were used to relieve feelings of stress. Turunen et al. (2005) identified a group of individuals who reported using analgesics frequently, but simultaneously reported having pain symptoms very rarely. Chrischilles et al. (1990) found that the vast majority of elderly men and women who used OTCA reported mild or no pain whatsoever. Andersen et al. (2009) found that not all medicine use for headache was explained by prevalence of symptoms. In our study, approximately 11% of women and 10% of men who reported no symptoms had used OTCA within the last 14 days. In epidemiological studies of OTC medicine, primarily analgesics, exposure to bullying, alcohol and illegal drug use and psychological symptoms such as depression and anxiety have been associated with medicine use, see e.g., (Abbott and Fraser 1998; Andersen et al. 2006; Due et al. 2007. Andersen et al. (2006) found medicine use clustered with smoking and drunkenness among adolescents and suggested that medicine use is part of a behavioral pattern of substance use to relieve stress.

Our study is cross sectional and does not allow causal interpretation; but there are several possible explanations for how stress may contribute to OTCA use. Perceived stress is associated with physiological processes that may permanently lower the threshold for experiencing health complaints (Ursin 1997). Hence, the association between stress and OTCA use may be mediated by stress-related symptoms. OTCAs are used primarily to treat headaches (Abbott and Fraser 1998; Antonov and Isacson 1998); and headache and stress are associated (Yokoyama et al. 2009). In analyses adjusted individually for symptoms, headache was the symptom that most notably attenuated the association between stress and OTCA use for men and women in all three surveys. Headache may be an important confounder of the association between stress and OTCA use, but we cannot exclude that headache may be a mediating factor between stress and OTCA use.

Women use analgesics more often than men (Antonov and Isacson 1998; Eggen 1994) and suffer more frequently from headaches and other subjective health complaints (Ekholm et al. 2006). One possible interpretation could be that more women use analgesics because they experience stress to a greater extent, which in turn might also result in more headaches and other subjective health complaints. However, in 1994, significantly more women felt stress in their daily lives, experienced headaches, and used OTCA compared to men, but stress and OTCA use were not associated.

Although there were no statistically significant differences in the association between stress and OTCA use across the three surveys, differences were found on visual inspection. The association between stress and OTCA use was not seen among women in 1994, while in 2000 and 2005 there was a significant and graded association between stress and OTCA use. It has been suggested that medicine use may be a way of gaining control, not just of physiological symptoms, but of everyday life in general, and that increasing medicine use may reflect a growing need for control in an ever more uncontrollable world (Whyte et al. 2002). There was a significant increase in OTCA use and reports of often feeling stressed between 1994 and 2005; hence, the public health impact of OTCA use to treat stress may have been greater in 2005 than in 1994.

Stress needs to be handled appropriately, i.e., dealing with underlying causes, as a constant level of stress can have serious health consequences such as reducing immune competence (Schneiderman et al. 2005). Among men, a high level of perceived stress is associated with higher all-cause mortality (Nielsen et al. 2008b).

There were significantly fewer participants with less education in 2005 compared to that in 1994. The association between stress and OTCA use barely changed in analyses adjusted for education.

There was a significant increase in all symptoms among women from 1994 to 2005 and almost all symptoms among men. This may be due to a change in the way data were collected in 2005: instead of being shown a card with all the pains and discomforts listed, respondents were asked about each symptom separately. The prevalence of all indicators for illness and health usually increases in step with the detail of the questioning. It is difficult to distinguish between methodological problems and development, but for some of the symptoms, the development between 2000 and 2005 seems to be a continuation of the development from 1987 to 2000 (Ekholm et al. 2006), and can therefore probably be interpreted as a genuine rise in the symptom prevalence. This is true for the prevalence of pain and discomfort in the arms, hands, legs, knees, hips or joints (Ekholm et al. 2006). In our study population, we saw a higher prevalence of headache among women in 2000 compared to 1994, and we therefore suggest that rise in headache prevalence among the 25 to 44-year-old women between 1994 and 2005 is genuine and not caused by methodological limitations.

The study was appropriate for the conducted analyses since it included three large nationally representative samples. Data were characterized by a vast exposure contrast that is advantageous when studying potential exposure–outcome associations. Most of the questions used in the present study are standard questions in health surveys (WHO 2003).

The study also has limitations. Cross-sectional surveys have limitations concerning causal interpretations. There is a risk of selection bias because individuals with whom contact was not obtained may have a higher prevalence of both stress and OTCA use. In that case, we are likely to have underestimated the associations between stress and OTCA use. The response rate between 1994 and 2005 diminished. Declining response rates in surveys is a matter of great concern in most western countries (Bay 2009). There are several possible reasons for the declining response rate in the Danish Health Interview Surveys. The increasing number of surveys in Denmark is most likely an important reason for the increasing refusal rates. An additional reason could be that the total length of the questionnaire has increased substantially over the years. The response rate alone is often a poor indicator of non-response bias. If non-response is not associated with the variables of interest, the non-response might not impact on the representativeness of the survey. However, if non-response is systematically associated with the variables under study, the non-response cannot be ignored. Previous studies on non-response in the Danish Health Interview Surveys have showed that the general validity of the results may not be threatened by the bias produced by non-response (Gundgaard et al. 2008; Kjoller and Thoning 2005).

We cannot rule out the possibility of residual confounding because perceived stress and use of OTCA may be influenced by a variety of exposures not included in this study. It is possible that the concomitant use of tranquillizers or anti-depressants interferes with the association between OTCA and stress, and this could also interfere with the time trend observed. The participants who were between 25 and 44 years of age in 1994, 2000 and 2005 may have grown up under different conditions and we cannot rule out that our results were affected by an age–period cohort effect. There is no time reference to the stress item; however, we believe that individuals know if they generally feel stressed or not, and a short time reference may have been less appropriate to measure generally perceived stress, as a holiday or an unusually busy period could affect the response.

Further research is needed to better understand the processes that connect stress and OTCA use. The association between stress and OTCA use should also be studied in other age groups, as the association may differ from one age group to another. Policy makers, health-care professionals and those in charge of dispensing medicines need to be aware that OTCAs are used beyond indication to treat stress.

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Conflicts of interest The authors declare that they have no competing interests.

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